

EXHIBIT B

BIODEGRADABLE HYDROGELS FOR DRUG DELIVERY

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in Eastern Time

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van der Waals forces and mer chains is great, it may be that the hydrogen bonding of cellulose is so strong and after hydration, the 1/ or the polymer backbone is hydrolyzed to result in ed polymers, the polymer mer the polymer backbone, s of the polymer chains leads systems, the reduction in the loss of coherence between weight degradation products from the body [29].

polymers dissolve in water. ylic acid), poly(styrene sul- readily dissolve in water by ter molecules. Other polar oly(ethylene oxide) (PEO), o readily dissolve in water by ss.

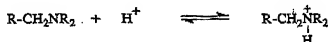
the hydrophilic polymer in hydrogel [28]. This hydrogel nposition [31]. Once a gel is ough a rather loose network on further addition of water, individual polymer molecules ally referred to as erosion or rd the core and finally the gel he dissolution rate of water- molecular weight and stereo-

depends on the amount of water, i the concentration of polymer concentration at which the gel polymer. At a given polymer i and vice versa by varying the ure, pH, or type of salt.

2.2.2 Charge Formation Followed by Dissolution

2.2.2.1 IONIZATION OR PROTONATION

Some polymers are initially water-insoluble but become solubilized by ionization or protonation of a pendant group. Examples are shown here.



Insoluble

Highly soluble

The solubility of polyacids is strongly pH-dependent. At low pH solution, polyacids are not water-soluble because the carboxyl groups of polyacids are protonated, i.e., not ionized. Upon an increase in the pH of the solution, the carboxyl groups release hydrogen atoms and become ionized. As the content of the ionized groups gradually increases, the polymer becomes more hydrophilic, absorbs water, swells, and finally dissolves in water. The solubility of polybases also strongly depends on pH, but the trend is opposite to that of polyacids. Polybases are water-soluble at low pH ranges.

Polyacids have been used widely as enteric coating materials for pharmaceuticals. They are poorly water-soluble in low pH environments, such as in the stomach, and dissolve in alkaline conditions such as those found in the intestines. The pH-sensitive polymers that have been used as enteric coating materials are shellac (esters of aleuritic acid), cellulose acetate phthalate, cellulose acetate succinate, poly(vinyl acetate phthalate), hydroxypropylmethylcellulose phthalate, and poly(methacrylic acid-co-methyl methacrylate) [32]. Among these, the most widely used polymers for enteric coating are cellulose acetate phthalate, poly(vinyl acetate phthalate); and poly(methacrylic acid-co-methyl methacrylate) [33,34]. The structures of these enteric coating polymers are shown in Figure 2.1. Cellulose acetate phthalate becomes water-soluble at a pH greater than 6, while poly(vinyl acetate phthalate) and hydroxypropylmethylcellulose phthalate are ionized at a lower pH [35].